APPENDIX E: Final Office Action of July 5, 2001

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/674,311	07/01/96	OLOPADE	ARSB:509--1

EXAMINER	
ART UNIT	PAPER NUMBER
1655	28

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Resp. to Prov'l Adv. Action 9/5/01
FINAL REJCTION Due 10/5/01
FINAL 11/5/01
12/5/01
01/05/02
Not of Appeal- 10/5/01
FIN. Not of App- 1/5/02

Office Action Summary

Application No.	Applicant(s)
08/674,311	Olopade et al
Examiner	**Art Unit**
Lisa Athur	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 16, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39-94* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39-94* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

1. This action is in response to the paper filed April 16, 2001 Currently claims 39-94 are pending. All of the arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. Any rejections which have not been reiterated have been withdrawn. This action is FINAL.

MAINTAINED REJECTIONS

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-50,52,53,59, 67-76,78,80-83,88-94 are rejected under 35 U.S.C. 102(b) as being anticipated by Kamb et al. (1994).

Kamb et al. teach isolated polynucleotides containing the tumor suppressor gene MTS1 which maps to 9p21-22. The cosmid that contains MTS1 of Kamb et al also contains the human methylthioadenosine phosphylase gene (MTAP) since these two genes are tightly linked. Thus the cosmid of Kamb et al is an isolated polynucleotide comprising the sequence of SEQ ID no 1 which is a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO 2. Necessarily then, the polynucleotide of Kamb et al. Comprises at least 21, 30, 40 or all contiguous bases from nucleotides 122-970 of SEQ ID NO 1 (limitations of claims 40-43). Since the polynucleotide of Kamb et al. Encodes the MTAP gene, it inherently meets the limitations of claims 45 and 46 that the encoded polypeptide promotes melanoma senescence and

suppresses glioma cell tumor generation. The cosmid used in Kamb et al. was at least 849 base pairs in length since it contains the CDKN2 which is target than 849 base pairs (limitations of 47-49). Kamb et al teaches a method for detecting a nucleic acid comprising a sequence encoding MTAP by hybridization with a probe comprising at least 21 bases of SEQ ID NO 1 because Kamb et al. Teaches a Southern blot (Figure 2) was performed using human genomic DNA and a probe which was a cosmid which contains the MTAP gene. Therefore, a nucleic acid containing the MTAP would be detected by hybridization of the cosmid of Kamb et al since the same probe was used by Kamb et al. that was used in the claimed method (claims 78-83).

Response to Arguments

The response traverses the rejection on the following grounds. The response argues that Kamb et al. Did not identify, isolate or sequence a polynucleotide comprising a nucleic acid sequence from SEQ ID NO 1. The response further states that even if MTAP is comprised on cosmid C5, Kamb et al. did not disclose a polynucleotide compromising the sequence from SEQ ID NO. 1. The response states that conception of a gene requires isolation of the gene. The response states that prior to the disclosure of SEQ ID NO 1 there was no understanding of where the sequence encoding MTAP was located.

All of these arguments have been thoroughly reviewed but are deemed non-persuasive for the following reasons. The claims are drawn to an isolated polynucleotide comprising a sequence region that encodes a polypeptide comprising the amino acids sequence of SEQ ID NO 2 or comprising fragments of SEQ ID NO 1. Because of the way the claims are written, the claims

encompass any isolated polynucleotide of any size which contains somewhere within its sequence a region that encodes SEQ ID NO 2 or contains the recited fragments of SEQ ID NO 1. The claims are not limited to a polynucleotide which encodes only SEQ ID NO 2 or which contains only the recited fragments of SEQ ID NO 1. As written the recited sequences can be embedded within much large isolated polynucleotides such as the isolated cosmid C5 polynucleotide. There is no argument that Kamb et al. Does not teach an isolated polynucleotide consisting of only the MTAP coding sequence but the none of the rejected claims are limited to such an embodiment. Determining the nucleotide sequence of a known polynucleotide does not distinguish the polynucleotide from that of the prior art because the nucleotide sequence is an inherent characteristic of any polynucleotide. Because Kamb et al. Teach a large isolated polynucleotide which contains somewhere within its structure the nucleic acid sequence encoding the MTAP polypeptide, Kamb et al. have in fact taught the isolation of a polynucleotide containing SEQ ID NO 1 and consequently, have "conceived" of the claimed polynucleotide even though Kamb et al. Certainly has not defined the specific position of MTAP or a polynucleotide consisting of SEQ ID NO 1 or fragments of SEQ ID NO 1. Therefore, this rejection is maintained.

Claims, 54-66, 74-76, 78-83, 88-94 are rejected under 35 U.S.C. 102(b) as being anticipated by Nobori et al.

Nobori et al. teach that a methylthioadenosine phosphylase cDNA was isolated and used to probe a human lambda-phage cDNA library and a 2000 base pair fragment was found to

contain the 3' end of the MTAP gene (page 753, col. 2, paragraph 3). This sequence was used as a probe for chromosome walking, I .e. in a hybridization detection reaction. The MTAP HinDIII fragment was inserted into a vector and transformed into a host cell page 754). It is noted that Nobori et al. Only discloses a 3' fragment of the human MTAP gene. However, the claims as written read on polynucleotides containing fragments of the MTAP gene as small as 10 bases.

Response to Arguments

The response traverses the rejection on the following grounds. The response argues that since physical map of the cDNA containing the 3' end of the MTAP gene shown in the Nobori et al. (1994) references is incorrect, the ordinary artisan would have been lead to look in the wrong place for a polynucleotide comprising SEQ ID NO 1. The response also argues that Nobori et al. Only teach a small fragment of the MTAP gene and did not teach the sequence of this fragment. The response argues that Norbori et al. did not characterize, isolate or sequence a polynucleotide comprising SEQ ID NO 1 and that the aim of their paper was to study a completely different gene.

Again the response cites *Amgen Inc v. Chugai Pharmaceutical Co., Ltd.* as evidence that Nobori et al. Did not teach a polynucleotide comprising SEQ ID NO 1 because they do not teach the isolation of sequencing of this nucleic acid and do not mention kits or methods of using the polynucleotide.

All of the arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. Claims 54-66 are broadly drawn to a nucleic acid of from 850-10,000

bp comprising a gene encoding a MTAP polypeptide which polypeptide comprises a region of 10, 20, or 30 amino acids from SEQ ID NO. 2. Since Nobori et al. Teach a 2000 base pair nucleic acid containing the 3' end of the MTAP gene which encodes the COOH end of the MTAP polypeptide, Norbori et al. Teach nucleic acids which meet all the limitations of the claims. The fact that Nobori et al. Do not teach the nucleotide sequence of the 3' end of the MTAP gene does not obviate the fact that they were in possession of a nucleic acid which encodes an MTAP polypeptide fragment. The determination of the nucleotide sequence of a known nucleic acid does not make the nucleic acid patentable over the prior art because the sequence is an inherent characteristic possessed by the nucleic acid of Nobori et al. Therefore, for these reasons the rejection is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39-42,45-66,74-75,77-83,88-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nobori et al. For the reasons given in the previous action.

Response to Arguments

The response argues that since physical map of the cDNA containing the 3' end of the MTAP gene shown in the Nobori et al. (1994) references is incorrect, the ordinary artisan would have been lead to look in the wrong place for a polynucleotide comprising SEQ ID NO 1.The response alleges, therefore, that Nobori et al. teach away from the present invention. The response asserts that the MTAP probe of Nobori et al. only meets an obvious to try standard and does not meet the prima facie obvious test. The response argues that since Nobori et al. Did not teach the nucleotide sequence of the full length MTAP gene, the reference does not teach that they were in possession of the MTAP gene prior to the present invention. The response cites *in re Eli Lilly & Co.* and *in re Deuel* to show that Nobori is insufficient as a reference.

All of the arguments have been thoroughly reviewed but are deemed non-persuasive for the following reasons. In general Applicant's arguments are directed to an embodiment to which the claims are not limited. There is no argument that Nobori et al. Does not teach the complete MTAP gene of SEQ ID no 1 encoding the a polypeptide of SEQ ID NO 2. However, the claims are not limited to such polynucleotides. Instead the claims 39-53 encompass a genus of polynucleotides which encode SEQ ID NO 2. That is, the polynucleotide can have a large number of different sequences as long as the encoded amino acid sequence is SEQ ID NO 2. Claims 54-76 are more broadly drawn to a very large genus of polynucleotides which do not have encode the full length MTAP gene and which can vary in sequence as long as they hybridize SEQ ID NO 1. Consequently, while the examiner is in agreement with Applicant over the non-obviousness of a polynucleotide consisting of SEQ ID NO 1, the probe of Nobori et al. would

have been expected by the ordinary artisan to detect the gene which it encodes, namely an MTAP coding sequence because Nobori et al. Specifically identified the fragments as the 3' end of the MTAP gene. The fact that the map of Nobori et al. Was incorrect would not have had any effect on the ability of the 2 kb HinDIII fragment to function as a probe in a hybridization assay on a cDNA library to have detected complementary clones. Chromosome walking is not the only method used to isolate a gene sequence and actually since Nobori et al. Already were in possession of the 3' end of the MTAP gene, the ordinary artisan would have seen that the easiest and quickest way to obtain the remainder of the gene would be to screen the cDNA library for overlapping clones.

Claims 84-87 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nobori et al. for the reasons of record.

Response to Arguments

The response traverses the rejection on the following grounds. Again the response argues that Nobori et al. Does not teach the nucleotide sequence of MTAP gene. And only teaches a 3' fragment of the MTAP gene and teaches the wrong map.

All of these arguments have been thoroughly reviewed but are deemed non-persuasive for the following reasons. The claims are drawn to a kit containing a nucleic acid segment of at least 21 bases from SEQ ID NO 1 and a detection reagent, and a restriction enzyme and another 21 bp fragment of SEQ ID NO 1. The fragment of Nobori is the 3' end of the MTAP gene which clearly

is a nucleic acid segment of at least 21 bases from SEQ ID NO 1. It is noted that the actual sequence of the fragment of Nobori et al. Was not taught. However, it is acknowledged by applicant and taught by Nobori et al. That the fragment of Nobori is the 3' end of the human MTAP gene and that SEQ ID NO 1 is the full length coding sequence of the human MTAP gene. Consequently, the ordinary artisan would have expected the Nobori et al. fragment to have the same sequence as the 3' end of SEQ ID NO 1. The fact that the map of Nobori et al. Was incorrect would not have had any effect on the ability of the 2 kb HinDIII fragment to function as a probe in a hybridization assay on a cDNA library to have detected complementary clones. Therefore, for these reasons, the rejection is maintained.

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Wednesday from 7:00 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

July 2, 2001